study that there were no renal hemodynamic differences between diuretics and ultrafiltration.

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Reply

We appreciate the enthusiastic interests and insightful comments regarding our report on the potential role of venous congestion as a driver for worsening renal function (WRF) in patients admitted with advanced decompensated heart failure (ADHF) (1). We have acknowledged in the report that many factors can contribute in the pathophysiology of WRF in the setting of ADHF. While our existing data cannot demonstrate direct causation between elevated central venous pressure and WRF, our current treatment goals are to reduce filling pressures and to improve cardiac output using a wide range of drug and device therapies according to protocols established in our heart failure intensive care unit. It is important to clarify that the mean dosages of furosemide during intensive medical therapy were similar among patients who did and did not develop WRF, with similar percentages of patients in both groups receiving furosemide through continuous parental infusion. While the biggest hemodynamic determinant of the subsequent development of WRF in this patient population with initially depressed cardiac index appeared to be elevated central venous pressure rather than low cardiac output, we believe our data supported the presence of venous congestion as the driver of the process, either due to underlying restrictive physiology, overzealous diuretic use, neurohormonal up-regulation, or more likely the severity of congestion. Dissecting these factors may be challenging in the clinical setting, and may vary widely among individual patients. Regardless, this is a clear departure from the traditional "cardiocentric" concept of impaired cardiac output as the primary determinant of cardio-renal compromise in some patients with ADHF.

Contrary to animal experiments, we did not observe a direct correlation between baseline renal function and severity of venous congestion; several reasons might account for this discrepancy. First, the duration and onset of venous congestion in the quoted animal experiments always was acute and short-lived while in patients admitted with ADHF venous congestion most often arises slowly and gradually over the preceding weeks. Second, some of our patients have been treated with long-term neurohormonal antagonists and may have pre-existing/intrinsic renal dysfunction contrary to animal models, which had normal renal function at the moment venous pressure was artificially raised. Furthermore, other extrinsic factors as a result of long-term venous congestion (such as raised intra-abdominal pressure caused by visceral edema or ascites) may contribute to this cardio-renal pathophysiology (2). However, the first step is to recognize that venous congestion is a major feature of the syndrome, which is the primary message of this and several other recent papers in different patient populations (3,4). We fully agree that more rigorous studies are needed, and we believe that the search for future ADHF therapies should focus on strategies that allow safe and optimal reduction *and* prevention of venous congestion to prevent such a devastating complication.

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Reply

We appreciate the opportunity to answer the thoughtful letter of Drs. Maqsood and Szerlip, who raised the issues of the role of vigorous diuresis in the patients discussed in the article by Mullens et al. (1), and the activation of the renin-angiotensin-aldosterone system (RAAS) after ultrafiltration (2).

Our interpretation of the study by Mullens et al. (1) is that the central venous pressure decrease in the worsening renal function (WRF) group was not significantly different from that of the non-WRF group, approximately 35%. Nevertheless, the central venous pressure remained significantly ($p = 0.04$) higher in the WRF group. We think this supports the hypothesis proposed by Mullens et al. (1) about the important role of venous congestion in contributing to WRF.

Our suggestion about the differing activation of the RAAS with diuretics and ultrafiltration is derived from an elegant study done over a decade ago. In 1994, Agostoni et al. (3) demonstrated that

in heart failure patients treated with either ultrafiltration or diuretics to achieve equivalent fluid removal, sustained hemodynamic and neurohormonal benefit occurred only in the ultrafiltration group. Compared with the diuretic group, patients treated with ultrafiltration had lower norepinephrine, plasma renin, and aldosterone levels for up to 90 days. Lower RAAS activation was associated with sustained improvement in objective measures of functional capacity. The rate of 14 to 15 ml/min for interstitial fluid mobilization was outlined still earlier by Fauchald and Fauchald (4), as recently reviewed by Schrier (5).

The conclusions of Rogers et al. (6) about the impact of diuretics and ultrafiltration on renal function might or might not be verified in larger trials. However, we feel strongly that the important outcomes in subsequent studies involving patients hospitalized with heart failure remain focused on a reduction of cardiovascular mortality and heart failure rehospitalizations, rather than on the more specific end point of renal function. This is where we propose that new tactics are needed.

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Is it Myocarditis or Arrhythmogenic Right Ventricular Cardiomyopathy?

Pieroni et al. (1) conclude that right ventricular myocarditis frequently mimics arrhythmogenic right ventricular cardiomyopathy (ARVC), and 3-dimensional electroanatomic mapping (guided endomyocardial biopsy is a tool that can differentiate the 2 entities, guiding appropriate therapy. The gist of their message suggests that these 2 entities are mutually exclusive, and in their cohort, electrocardiographic abnormalities, arrhythmias, right ventricular structural and functional abnormalities, Task Force criteria fulfillment, a 3-dimensional voltage map, and inducible arrhythmias on electrophysiologic testing could not separate the wheat from the chaff. Some experts have suggested that a "hot phase" may interpolate periods of clinical quiescence, and the former may present as myocarditis or worsening ventricular arrhythmia (2). If we were to acknowledge the possibility of this alternative hypothesis, the findings may be interpreted differently. The 15 patients who were diagnosed with myocarditis may represent a hot phase, and although they did not have fibrofatty changes, they fulfilled Task Force criteria, which are quite specific for the diagnosis of the disease. These patients with myocarditis may represent an earlier phase of the disease, and the observation that none of these patients experienced arrhythmic events gives credence to this possibility. Genetic testing in this sample would have been highly desirable even though it is not considered necessary for diagnosis by the authors. We agree with the authors that a revision and reappraisal of diagnostic criteria for ARVC is long overdue.

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Myocarditis Mimicking Arrhythmogenic Right Ventricular Cardiomyopathy

We have read with interest the paper by Pieroni et al. (1) addressing myocarditis as a common differential diagnosis to arrhythmogenic right ventricular cardiomyopathy (ARVC). Among 30 patients noninvasively fulfilling Task Force criteria (2) for ARVC, they found that 15 patients actually had myocarditis based on 3-dimensional electroanatomic voltage mapping-guided endomyocardial biopsy. Voltage-guided biopsy is an elegant way of obtaining histological material from areas of the right ventricle with electrical signs of regional abnormalities and may facilitate the diagnostic workup. However, we have the following questions/concerns about the study by Pieroni et al. (1):